

10/713,394

=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

L1 21366 S ACID (W) (RESISTANT OR STABLE)
L2 515920 S PROTEASE?
L3 85 S L1(W)L2
L4 44 DUP REM L3 (41 DUPLICATES REMOVED)
L5 6 S (CEREAL OR NUTRI? OR (PROTEIN (W)SOURCE)) AND L4
L6 1048 S NOCARDIOPSIS###
L7 130 S L2 AND L6
L8 8 S L1 AND L7
L9 4 DUP REM L8 (4 DUPLICATES REMOVED)
E SJOEHOLM C/AU
L10 37 S E3-E4
E OESTERGAARD P R/AU
L11 49 S E3-E9
L12 76 S L10 OR L11
L13 6 S L3 AND L12
L14 4 DUP REM L13 (2 DUPLICATES REMOVED)

=>

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NEWS 6 MAY 21 TOXCENTER enhanced with BIOSIS reload
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NEWS 8 MAY 22 CA/CAPplus enhanced with IPC reclassification in Japanese patents
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NEWS 13 JUL 02 LMEDLINE coverage updated
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NEWS 15 JUL 02 CHEMCATS accession numbers revised
NEWS 16 JUL 02 CA/CAPplus enhanced with utility model patents from China
NEWS 17 JUL 16 CAPplus enhanced with French and German abstracts
NEWS 18 JUL 18 CA/CAPplus patent coverage enhanced
NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
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NEWS 22 AUG 06 BEILSTEIN updated with new compounds
NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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| | ENTRY | SESSION |
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FILE 'LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007
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=> s acid (w)(resistant or stable)
L1 21366 ACID (W)(RESISTANT OR STABLE)

=> s protease?
L2 515920 PROTEASE?

=> s l1(w)l2
L3 85 L1(W) L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 44 DUP REM L3 (41 DUPLICATES REMOVED)

=> d 1-44 ibib ab

L4 ANSWER 1 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:307362 BIOSIS
DOCUMENT NUMBER: PREV200600314107
TITLE: Use of acid-stable subtilisin proteases in animal feed.
AUTHOR(S): Sjoeholm, Carsten [Inventor]; Oestergaard, Peter Rahbek
[Inventor]; Klunter, Anna-Marie [Inventor]
CORPORATE SOURCE: Allerod, Denmark
ASSIGNEE: DSM IP Assets B. V
PATENT INFORMATION: US 06960462 20051101
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (NOV 1 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2006
Last Updated on STN: 14 Jun 2006

AB Acid-stable proteases of the subtilisin family, their use in animal feed, feed-additives and feed compositions containing such proteases, and methods for the treatment of vegetable proteins using such proteases.

L4 ANSWER 2 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:548417 BIOSIS
DOCUMENT NUMBER: PREV200510345270
TITLE: Use of acid-stable proteases
in animal feed.
AUTHOR(S): Sjoeholm, Carsten [Inventor]; Oestergaard, Peter Rahbek
[Inventor]
CORPORATE SOURCE: Alleroed, Denmark
ASSIGNEE: F. Hoffman-La Roche AG
PATENT INFORMATION: US 06855548 20050215
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (FEB 15 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005

AB Acid-stable proteases homologous to those derived from strains of the genus Nocardiosis, their use in animal feed, feed-additives and feed compositions containing such proteases, and methods for the treatment of vegetable proteins using such proteases.

L4 ANSWER 3 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1094196 HCAPLUS
DOCUMENT NUMBER: 143:466149
TITLE: Capsule compositions containing multiple
anti-inflammatory enzymes
INVENTOR(S): Zheng, Changxue; Yang, Yabo; Huang, Wei
PATENT ASSIGNEE(S): Beijing Aolute Biomedicine Research and Development
Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|------------------|----------|
| CN 1562359 | A | 20050112 | CN 2004-10030648 | 20040402 |
| PRIORITY APPLN. INFO.: | | | CN 2004-10030648 | 20040402 |

AB The title capsules are manufactured from one or more anti-inflammatory enzymes, and auxiliary materials. The enzymes includes acid-resistant RNase, acid-resistant protease, acid protease, bromelain, papain, trypsin, chymotrypsin, superoxide dismutase, serratiopeptidase, seaprose, pronase, lysozyme, and subtilisin. The invention has the advantages of retained enzymic activity, good stability, reasonable formulation, etc.

L4 ANSWER 4 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:1742 BIOSIS
DOCUMENT NUMBER: PREV200500011483
TITLE: Dietary supplements containing natural ingredients.
AUTHOR(S): Perkes, Lynn [Inventor, Reprint Author]
CORPORATE SOURCE: ASSIGNEE: Melaleuca, Inc.
PATENT INFORMATION: US 6818233 20041116
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (Nov 16 2004) Vol. 1288, No. 3.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.

ISSN: 0098-1133 (ISSN print).

DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004

AB The invention provides a dietary supplement comprising at least one flavonoid source and an enzyme, that is effective for inhibiting in vivo platelet activity and LDL cholesterol oxidation in a mammal at a dosage of about 30 mg/Kg or less. The supplement may contain flavonoid sources found in grape seed extracts, grape skin extracts, bilberry extracts, ginkgo biloba extracts or the flavonoid quercetin. The supplement may also contain fungal proteases, acid stable proteases and bromelain. The invention further provides a method for using the dietary supplement and an article of manufacture containing the supplement.

L4 ANSWER 5 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:19297 BIOSIS

DOCUMENT NUMBER: PREV200400011181

TITLE: Urinastatin as an Indicator of Stress Response to Various Surgical Procedures. (Comparison of Urine Urinastatin Amounts among Post-Operative Patients).

AUTHOR(S): Nagashima, Kimimoto [Reprint Author]; Takeda, Miwako [Reprint Author]; Fujimoto, Kazuhiro [Reprint Author]; Takahata, Osamu [Reprint Author]; Iwasaki, Hiroshi [Reprint Author]

CORPORATE SOURCE: Anesthesiology, Asahikawa Medical College, Asahikawa, Hokkaido, Japan

SOURCE: Anesthesiology Abstracts of Scientific Papers Annual Meeting, (2003) No. 2003, pp. Abstract No. A-544.
<http://www.asa-abstracts.com>. cd-rom.
Meeting Info.: 2003 Annual Meeting of the American Society of Anesthesiologists. San Francisco, CA, USA. October 11-15, 2003. American Society of Anesthesiologists.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

AB Introduction Urinastatin (UTI) molecular weight of about 24,000 that exists naturally in the human body and purified from urine. UTI is a protease inhibitor of various enzymes such as trypsin, alfa-chymotrypsin, leukocyte elastase, plasmin, and cathepsinG. UTI is also referred as HI-30, acid-stable protease inhibitor or bikunin. Because UTI stabilizes lysosomal membranes by suppressing release of lysosomal enzymes, UTI plays an important role in host defense during pathological stress. Thus, UTI is approved for the treatment of acute pancreatitis and circulatory shock and sepsis induce Ialpha-TI (Inter-alpha- trypsin inhibitor) in the liver. Ialpha-TI is then converted to UTI by activated neutrophilic elastase. Accordingly, UTI can be used as an indicator of surgical stress. Replacement of conventional invasive surgical procedures with advanced less invasive one in the last decade has led surgical operators to reevaluate the peri-operative managements for surgical stress responses. However, to date there is no direct comparison of urine UTI amounts after different procedures for cardiac and gastric surgeries. Materials and methods We measured urine UTI amounts during postoperative period of cardiac surgery and gastric surgery. In the cardiac surgery, patients were divided into the use of cardio pulomnary bypass group (On Pump; n = 6) and no use of cardio pulmonary bypass group (Off Pump; n = 6). In the gastric surgery, patients were divided into laparotomy group (Op; n = 10 and laparoscopic group (Lp; n=7) Urine speciments were collected prior to surgical operation (Pre-ope) and at the post-operative day (POD) 1,3,5, and 7 from the patients in the morning (8 am to 10 am). The anesthetic procedures were consistent

between groups. UTI amounts were determined by ELISA method and corrected by creatinin levels measured at the same time. Statistics Statistical analysis was performed using Kruskal-Wallis test. All of the data were expressed as mean \pm SD. Differences were considered statistically significant at $p < 0.05$. Results The urine amounts were elevated the most at POD3 in all patients. In cardiac surgery patients, UTI amounts (U/g) on POD 7 was 902 \pm 148 in On Pump Group ($n = 6$), and 353 \pm 116.1 in Off Pump Group ($n = 6$). At POD7, UTI of On Pump Group remained elevated significantly compared to UTI of Off Pump Group. In gastric surgery patients, UTI amounts (U/g) at POD 3, 5, 7 were 2590 \pm 2494, 2511 \pm 3331, 1324 \pm 1497, respectively, in Open Group ($n = 10$), whereas 980 \pm 387, 649 \pm 285, 459 \pm 243, respectively in Lp Group ($n = 7$). UTI levels in Open Group remained elevated significantly compared to its levels in Lp Group on POD 3, 5, 7. Conclusion Urine UTI amounts after conventional, invasive surgeries were significantly higher than those following less invasive surgeries with advanced techniques. If UTI is critical for host defense, further additional supplement of UTI during a perioperative period may be beneficial to protect patients from surgical stress. Anesthesiology 2003; 99: A544.

L4 ANSWER 6 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1

ACCESSION NUMBER: 2001-16039 BIOTECHDS

TITLE: Use of acid stable protease for
producing a food composition;
for use as feedstuff, as a food-additive and in vegetable
protein treatment

AUTHOR: Oestergaard P R; Sjoeholm C

PATENT ASSIGNEE: Roche

LOCATION: Basle, Switzerland.

PATENT INFO: WO 2001058276 16 Aug 2001

APPLICATION INFO: WO 2001-EP1153 5 Feb 2001

PRIORITY INFO: DK 2000-200 8 Feb 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-488930 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where the protease has identity of at least 70% to a 188 amino acid sequence (I) and or a 17 amino acid sequence (II), is claimed. Also claimed are: improving the nutritional value of feedstuff; an animal food-additive; and treatment of vegetable proteins. At least one acid stable protease is useful in the preparation of a composition for use in feedstuff. The protease has 71% identity to (I) and/or (II). The dosage of the protease is 0.01-200 mg. The feed composition is useful for feeding animals, including humans. Animals include ruminants and non-ruminants i.e. monogastric animals i.e. pigs, poultry and fish. The feedstuff comprises phytase, endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase (EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable source. (49pp)

L4 ANSWER 7 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 2

ACCESSION NUMBER: 2001-16038 BIOTECHDS

TITLE: Use of acid stable protease of
the subtilisin for producing a food composition;
for use as feedstuff, as a food-additive and in vegetable
protein treatment

AUTHOR: Oestergaard P R; Sjoeholm C; Klunter A

PATENT ASSIGNEE: Roche

LOCATION: Basle, Switzerland.

PATENT INFO: WO 2001058275 16 Aug 2001

APPLICATION INFO: WO 2001-EP1152 5 Feb 2001

PRIORITY INFO: DK 2000-200 8 Feb 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-488929 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where the protease is of the subtilisin family and/or has less than 10% residual activity when inhibited with subtilisin, is claimed. Also claimed are: improving the nutritional value of feedstuff; an animal food-additive; and treatment of vegetable proteins. At least one acid stable protease is useful in the preparation of a composition for use in feedstuff. The protease is of the subtilisin family and/or 10% residual activity when inhibited with subtilisin. The dosage of the protease is 0.01-200 mg/kg of feed. The feed composition is useful for feeding animals, including humans. Animals include ruminants and non-ruminants i.e. monogastric animals i.e. pigs, poultry and fish. The feedstuff comprises phytase, endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase (EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable source. (63pp)

L4 ANSWER 8 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:130591 HCAPLUS

DOCUMENT NUMBER: 130:196123

TITLE: Dietary supplements containing natural ingredients

INVENTOR(S): Perkes, Lynn

PATENT ASSIGNEE(S): Melaleuca, Incorporated, USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|------------------|----------|
| WO 9907400 | A1 | 19990218 | WO 1998-US16181 | 19980805 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| TW 542721 | B | 20030721 | TW 1998-87112770 | 19980803 |
| CA 2244512 | A1 | 19990206 | CA 1998-2244512 | 19980805 |
| AU 9886868 | A | 19990301 | AU 1998-86868 | 19980805 |
| AU 731089 | B2 | 20010322 | | |
| EP 1009417 | A1 | 20000621 | EP 1998-938319 | 19980805 |
| EP 1009417 | B1 | 20061102 | | |
| R: | AT, CH, DE, ES, FR, GB, IT, LI, PT, IE | | | |
| JP 2001513332 | T | 20010904 | JP 2000-506989 | 19980805 |
| AT 344048 | T | 20061115 | AT 1998-938319 | 19980805 |
| US 6818233 | B2 | 20041116 | US 1998-194165 | 19981120 |
| US 2002048575 | A1 | 20020425 | US 1999-194165 | 19990511 |
| US 6818233 | B2 | 20041116 | | |
| MX 200001287 | A | 20011031 | MX 2000-1287 | 20000204 |
| HK 1027973 | A1 | 20070216 | HK 2000-107372 | 20001117 |
| US 2005089588 | A1 | 20050428 | US 2004-929332 | 20040830 |
| US 7229651 | B2 | 20070612 | | |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|----------|
| US 1997-907317 | A2 | 19970806 |
| WO 1998-US16181 | W | 19980805 |
| US 1999-194165 | A1 | 19990511 |

AB The invention provides a dietary supplement comprising at least one flavonoid source and an enzyme, that is effective for inhibiting in vivo platelet activity and LDL cholesterol oxidation in a mammal at a dosage of

about 30 mg/kg or less. The supplement may contain flavonoid sources found in grape seed exts., grape skin exts., bilberry exts., ginkgo biloba exts. or the flavonoid quercetin. The supplement may also contain fungal proteases, acid stable proteases and bromelain. The invention further provides a method for using the dietary supplement and an article of manufacture containing the supplement.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:1297 HCAPLUS
DOCUMENT NUMBER: 128:76856
TITLE: Nonaqueous gelled automatic dishwashing composition for removal of protein and starch residue on dish ware
INVENTOR(S): Gorlin, Philip A.; Kenkare, Divaker; Phillips, Steve
PATENT ASSIGNEE(S): Colgate-Palmolive Co., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 5698507 | A | 19971216 | US 1996-716812 | 19960910 |
| PRIORITY APPLN. INFO.: | | | US 1996-716812 | 19960910 |

AB Automatic dishwashing compns. containing a mixture of an acid-resistant protease enzyme and an acid-resistant amylase enzyme are very useful in the removal of protein and carbohydrate soils from dish ware at operating temps. of 100-140° F. The detergent composition comprised (a) 1-6% nonionic surfactant; (b) 5-15% citric acid; (c) 0.75-3% H2O2; (d) 0.25-3% ≥1 acid-resistant protease enzyme; (e) 0.25-3% ≥1 amylase enzyme; (f) 1-4% hydrotrope; (g) 0.1-1.5% CaCl2; (h) 0.5-2% Na formate; (i) 0.1-10% gelling system comprising a blend of hydroxypropyl cellulose and a swelling agent propylene carbonate; and (j) the balance water.

L4 ANSWER 10 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:658629 HCAPLUS
DOCUMENT NUMBER: 121:258629
TITLE: Molded block containing acid and protease for cleaning and deodorizing urinals
INVENTOR(S): Van Vlahakis, Eftichios; Manolas, John A.; Marrese, Michael J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 13 pp. Division of U.S. Ser. No. 9;960,55.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5336424 | A | 19940809 | US 1993-45939 | 19930412 |
| PRIORITY APPLN. INFO.: | | | US 1993-45939 | A3 19930412 |
| | | | US 1992-996055 | 19921223 |

AB The title composition contains an acid (e.g., H3PO4), an acid-stable protease, amphoteric and nonionic surfactants, and a germicide and is dispensed from a disposable dispenser which prevents direct contact of the block with urine but not with water during flushing of the urinal.

L4 ANSWER 11 OF 44 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 95146163 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7843802
TITLE: Immunohistochemical demonstration of bikunin, a light chain of inter-alpha-trypsin inhibitor, in human brain tumors.
AUTHOR: Yoshida E; Maruyama M; Sugiki M; Mihara H
CORPORATE SOURCE: Department of Physiology, Miyazaki Medical College, Japan.
SOURCE: Inflammation, (1994 Dec) Vol. 18, No. 6, pp. 589-96.
Journal code: 7600105. ISSN: 0360-3997.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 16 Mar 1995
Last Updated on STN: 16 Mar 1995
Entered Medline: 9 Mar 1995

AB The presence and localization of bikunin (HI-30, or acid-stable protease inhibitor), a light chain of inter-alpha-trypsin inhibitor, was examined in 30 brain tumors employing immunohistochemical methods. The brain tumors involved 13 kinds of histological diagnosis. Bikunin immunoreactivity was detected in all of the brain tumors examined. Fibrillary staining of the glial processes was observed in astrocytoma, oligodendroglioma, and schwannoma. Intracytoplasmic staining in the interstitial cells, reactive astrocytes, and macrophages was noted in medulloblastoma, ependymoma, and meningioma. Metastatic tumors demonstrated intense immunoreactivity in the tissues surrounding the tumor cells. Neuronal cells revealed no bikunin immunoreactivity. There was no correlation between the intensity of staining and histologic type or grading of malignancy. In view of our earlier report that bikunin was present in the connective tissues around the site of cancer invasion, the above findings suggest that bikunin may play an important role in defense or repair at the tissue destruction and degeneration site.

L4 ANSWER 12 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1994-08840 BIOTECHDS
TITLE: Solid-state fermentation of acid-resistant proteinase by *Aspergillus niger* var.;
protease production and optimization of culture conditions
AUTHOR: Yaoping X; Linlin Y; Yuying Q; Guanqian F; Dibo F
CORPORATE SOURCE: Zhejiang-Acad.Agr.Sci.Inst.Microbiol.
LOCATION: Institute of Microbiology, Zhejiang Academy of Agricultural Sciences, Hangzhou 310021, People's Republic of China.
SOURCE: Ind.Microbiol.; (1993) 23, 6, 16-20
CODEN: GOWEEK
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Culture medium and fermentation conditions were optimized for the production of acid-resistant protease by *Aspergillus niger* var. Number QX-066. A high enzymatic activity, 11674 U/g, was obtained on a solid medium consisting of high carbon and low nitrogen. Further experiments showed the activity could be increased on medium containing a suitable phosphate. The characteristics of the protease and the producing fungus were changed effectively is a proper enzyme-inducing medium was added to the solid medium on which the highest activity was produced. The optimum solid-state medium consisted of bran, bean cake, complex inorganic nitrogen, phosphate and enzyme-induced material. The activity produced on this medium reached 18316 U/g. The optimum fermentation temperature conditions were 28-30 deg for the first 30 hr, followed by a decrease in temperature to 25 deg. The highest fermentation temperature was controlled below 36 deg and the relative humidity was kept above 50 deg. Fermentation was carried out for 50 hr. (12 ref)

L4 ANSWER 13 OF 44 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 92120777 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 1769732
 TITLE: Acid-stable protease inhibitor in chronic phase of carrageenin-induced inflammation in rats.
 AUTHOR: Sugiki M; Maruyama M; Yoshida E; Sumi H; Mihara H
 CORPORATE SOURCE: Department of Physiology, Miyazaki Medical College, Japan.
 SOURCE: Inflammation, (1991 Aug) Vol. 15, No. 4, pp. 281-9.
 Journal code: 7600105. ISSN: 0360-3997.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199202
 ENTRY DATE: Entered STN: 15 Mar 1992
 Last Updated on STN: 3 Feb 1997
 Entered Medline: 21 Feb 1992

AB The activity and kinetics of acid-stable protease inhibitor (ASPI) were investigated in the chronic phase of carrageenin-induced inflammation in rats. The ASPI activity was 19.6 +/- 3.1 units/ml in the plasma and 15.4 +/- 2.1 units/ml in the inflammatory exudate. The plasma value was significantly higher than that of the control (11.6 +/- 1.3 units/ml). A kinetics study was performed using purified and radiolabeled rat plasma ASPI, whose NH2-terminal amino acid sequence was Ala-Val-Leu-Pro-Gln-Glu-Asn-Glu-Gly-X-Gly-Ser-Glu-Pro-Leu-Ile-Thr-Gly-Thr-Leu-Lys-Lys-Glu-Asp-Ser-Asn-Gln-Leu-Lys-Tyr-Ser-Glu-Gly-Pro. The half-life of the distributive phase was 4.3 +/- 0.4 min and that of the postdistributive phase (biological half-life) was 42.2 +/- 9.2 min in inflammation. There was no significant difference compared with the values in the control (3.9 +/- 0.4 min and 40.7 +/- 6.5 min, respectively). It appeared that the increase in ASPI in inflammation was not due to prolonged excretion of the inhibitor but to an increased production of it, and ASPI was rapidly distributed to the fluids and tissues.

L4 ANSWER 14 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 1992:60264 BIOSIS
 DOCUMENT NUMBER: PREV199242024164; BR42:24164
 TITLE: INHIBITORY PROPERTIES OF PARTIALLY PURIFIED ACID STABLE PROTEASE INHIBITOR FROM EXUDATE OF THE CHRONIC PHASE OF CARRAGEENIN-INDUCED INFLAMMATION IN RATS.
 AUTHOR(S): SUGIKI M [Reprint author]; MARUYAMA M; YOSHIDA E; SHIMAYA K; KAWABE K; MIHARA H
 CORPORATE SOURCE: DEP PHYSIOL, MIYAZAKI MED COLL, KIYOTAKE, MIYAZAKI-GUN, 889-16, JPN
 SOURCE: Japanese Journal of Physiology, (1991) Vol. 41, No. SUPPL, pp. S110.
 Meeting Info.: 68TH ANNUAL MEETING OF THE PHYSIOLOGICAL SOCIETY OF JAPAN, KYOTO, JAPAN, MARCH 27-29, 1991. JPN J PHYSIOL.
 CODEN: JJPHAM. ISSN: 0021-521X.
 DOCUMENT TYPE: Conference; (Meeting)
 FILE SEGMENT: BR
 LANGUAGE: ENGLISH
 ENTRY DATE: Entered STN: 21 Jan 1992
 Last Updated on STN: 21 Jan 1992

L4 ANSWER 15 OF 44 MEDLINE on STN DUPLICATE 5
 ACCESSION NUMBER: 92038403 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1936536
TITLE: Partial characterization of a unique mitogenic activity
secreted by rat Sertoli cells.
AUTHOR: Lamb D J; Spotts G S; Shubhada S; Baker K R
CORPORATE SOURCE: Scott Department of Urology, Baylor College of Medicine,
Houston, TX. 77030.
CONTRACT NUMBER: R01-DK39719 (NIDDK)
RR-05425 (NCRR)
SOURCE: Molecular and cellular endocrinology, (1991 Aug) Vol. 79,
No. 1-3, pp. 1-12.
Journal code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 3 Mar 2000
Entered Medline: 18 Dec 1991

AB Sertoli cell conditioned medium (SCCM) contains a potent mitogen, Sertoli cell secreted growth factor (SCSGF). A431 cells, derived from a human epidermoid carcinoma have provided an excellent model cell line for the study of this apparently unique activity secreted by rat Sertoli cells in vitro. Previously, it was shown that SCCM contained an epidermal growth factor (EGF)-like activity which was thought to be the mitogen for A431 cells. The present study showed that these two factors are distinct entities. The secretion of the EGF-like activity decreased with increasing number of culture days, while that of SCSGF and of another Sertoli cell specific protein, transferrin remained constant. The addition of SCCM stimulated whereas 2.5 ng/ml EGF inhibited the A431 cell growth. The proliferative response of A431 cells to a wide variety of growth factors and known Sertoli cell secretions was investigated. SCSGF was the only growth factor of known Sertoli cell secretions tested (transforming growth factors (TGF alpha, TGF beta), EGF, bombesin, fibroblast growth factor (FGF), platelet derived growth factor (PDGF), insulin-like growth factors 1 and 2 (IGF-1 and IGF-2), prostaglandins E-1 and E-2, insulin, transferrin and lactate) which stimulated A431 cell proliferation. SCSGF was mitogenic for A431 cells even in the presence of serum in the culture medium. The partially purified SCSGF was heat- and acid-stable, protease-sensitive with a molecular weight of 14,000. It did not bind to heparin or concanavalin A-Sepharose. The secretion of a mitogenic activity by the Sertoli cell which is different from other previously identified growth factors and which coincides with active spermatogenesis could have important implications in the regulation of spermatogenesis.

L4 ANSWER 16 OF 44 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 90130649 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2298817
TITLE: Secretion of a TGF-beta-like growth inhibitor by normal rat
mammary epithelial cells in vitro.
AUTHOR: Ethier S P; Van de Velde R M
CORPORATE SOURCE: Breast Cancer Group, Michigan Cancer Foundation, Detroit
48201.
CONTRACT NUMBER: CA 40064 (NCI)
SOURCE: Journal of cellular physiology, (1990 Jan) Vol. 142, No. 1,
pp. 15-20.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 28 Feb 1990

AB We have examined conditioned medium (CM) from cultures of normal rat mammary epithelial (RME) cells for growth factor activity on fresh RME cell cultures. RME cell-derived CM contained potent growth inhibitory activity toward fresh RME cell cultures when the medium was acidified by dialysis against 1% acetic acid prior to concentration. Dialysis of the CM at neutral pH resulted in CM that had growth stimulatory activity and no inhibitory activity. The acid-activated growth inhibitor was heat and acid stable, protease sensitive, and eluted from a Bio-Gel p60 column with a peak of activity in the 28 kDa range. Incubation of the acidified-concentrated CM with neutralizing antiserum (affinity purified IgG) against transforming growth factor (TGF)-beta completely abolished the inhibitory activity of the CM. Furthermore, RME cell growth in the presence of the growth inhibitor plus TGF-beta antiserum was greater than that observed in growth medium alone. Subsequent experiments demonstrated that addition of TGF-beta antiserum alone to serum-free medium enhanced RME cell growth, whereas addition of nonimmune IgG was without effect even at 25-fold higher concentrations. Zymographic analysis of RME-CM revealed the presence of plasminogen activator proteases that may mediate the partial activation of the latent growth factor. These results indicate that normal RME cells secrete a latent TGF-beta-like growth factor into conditioned medium. Furthermore, the results indicate that some of the latent growth factor is activated in situ and contributes to the growth potential of the cells in primary culture in an autocrine manner.

L4 ANSWER 17 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:437612 BIOSIS
DOCUMENT NUMBER: PREV199192093777; BA92:93777
TITLE: PARTIAL CHARACTERIZATION OF A UNIQUE MITOGENIC ACTIVITY
SECRETED BY RAT SERTOLI CELLS.
AUTHOR(S): LAMB D J [Reprint author]; SPOTTS G S; SHUBHADA S; BAKER K
R
CORPORATE SOURCE: DEP UROL, BAYLOR COLL MED, 1 BAYLOR PLAZA/ROOM 440E,
HOUSTON, TEX 77030, USA
SOURCE: Molecular and Cellular Endocrinology, (1990) Vol. 79, No.
1-3, pp. 1-12.
CODEN: MCEND6. ISSN: 0303-7207.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 26 Sep 1991
Last Updated on STN: 26 Sep 1991

AB Sertoli cell conditioned medium (SCCM) contains a potent mitogen, Sertoli cell secreted growth factor (SCSGF). A431 cells, derived from a human epidermoid carcinoma have provided an excellent model cell line for the study of this apparently unique activity secreted by rat Sertoli cells in vitro. Previously, it was shown that SCCM contained an epidermal growth factor (EGF)-like activity which was thought to be the mitogen for A431 cells. The present study showed that these two factors are distinct entities. The secretion of the EGF-like activity decreased with increasing number of culture days, while that of SCSGF and of another. Sertoli cell specific protein, transferrin remained constant. The addition of SCCM stimulated whereas 2.5 ng/ml EGF inhibited the A431 cell growth. The proliferative response of A431 cells to a wide variety of growth factors and known Sertoli cell secretions was investigated. SCSGF was the only growth factor of known Sertoli cell secretions tested (transforming growth factors (TGF α , TGF β), EGF, bombesin, fibroblast growth factor (FGF), platelet derived growth factor (PDGF), insulin-like growth factors 1 and 2 (IGF-1 and IGF-2), prostaglandins E-1.

and E-2, insulin, transferrin and lactate) which stimulated A431 cell proliferation. SCSGF was mitogenic for A431 cells even in the presence of serum in the culture medium. The partially purified SCSGF was heat- and acid-stable, protease-sensitive with a molecular weight of 14,000. It did not bind to heparin or concanavalin A-Sepharose. The secretion of a mitogenic activity by the Sertoli cell which is different from other previously identified growth factors and which coincides with active spermatogenesis could have important implications in the regulation of spermatogenesis.

L4 ANSWER 18 OF 44 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 88053799 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3677604
TITLE: Acid-stable protease
inhibiting polypeptides formed from denatured horse plasma
by proteolysis.
AUTHOR: Pellegrini A; Hageli G; von Fellenberg R
CORPORATE SOURCE: Department of Veterinary Physiology, University of Zurich,
Switzerland.
SOURCE: Comparative biochemistry and physiology. B, Comparative
biochemistry, (1987) Vol. 88, No. 1, pp. 237-42.
Journal code: 2984730R. ISSN: 0305-0491.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 21 Jan 1988
AB 1. Trypsin digestion of perchloric acid precipitated horse plasma yielded
polypeptides with inhibitory properties for trypsin, chymotrypsin and, to
a small extent, kallikrein. 2. The Mr of the inhibitory polypeptides were
73,000 and 24,000. 3. The number, enzyme specificity and Mr of the
inhibitory polypeptides differed from the values known for the human
being. 4. The inhibitory polypeptides were purified by affinity
chromatography on Sepharose-trypsin and by gel filtration through Sephadex
G-75. 5. Protease inhibitory polypeptides were generated in the same
manner by chymotrypsin, elastase, proteinase K, pronase, collagenase,
papain and subtilisin. 6. The number and electrophoretic migration of the
inhibitory polypeptides obtained with the different enzymes were variable.
7. The enzyme specificity was constant since all polypeptides inhibited
only trypsin, chymotrypsin and kallikrein to a small extent. 8. None of
the inhibitory polypeptides were immunologically related to native plasma
proteins or plasma protease inhibitors.

L4 ANSWER 19 OF 44 MEDLINE on STN
ACCESSION NUMBER: 88019372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3660733
TITLE: [Effective method of isolating an acid-
stable protease inhibitor from human
urine].
Effektivnyi metod vydeleniia kislotostabil'nogo ingibitora
proteinaz iz mochi cheloveka.
AUTHOR: Ogloblina O G; Belova L A; Malakhov V N
SOURCE: Voprosy meditsinskoi khimii, (1987 Jul-Aug) Vol. 33, No.
4, pp. 119-24.
Journal code: 0416601. ISSN: 0042-8809.
PUB. COUNTRY: USSR
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 29 Oct 1987

AB A modification is described of the previously developed procedure for isolation of acid stable proteinase inhibitor (ASI) from urine of patients with nephritis. The modified procedure enabled to increase the yield of the inhibitor and to obtain its highly purified preparations. These preparations possessed a property to inhibit effectively the activity of human granulocyte elastase ($k_i = 10(4) \text{ M}^{-1} \text{ min}^{-1}$). The modified procedure is based on affinity chromatography on chymotrypsin-Sepharose 4B, substitution of dialysis by gel filtration on Sephadex G-25, use of alternative methods for concentration of protein fractions instead of membrane ultrafiltration and chromatography on polyamide for ASI depigmentation. The inhibitor yield amounted up to 75% of the initial activity in urine. The possibilities of the human urine ASI use in medical practice are discussed.

L4 ANSWER 20 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1985-08801 BIOTECHDS
TITLE: Acid stable protease from
mutants of *Aspergillus niger*;
mutagenesis of the wild strain

PATENT ASSIGNEE: Henkel
PATENT INFO: US 4518697 21 May 1985
APPLICATION INFO: US 1982-449415 13 Dec 1982
PRIORITY INFO: DE 1981-149457 14 Dec 1981
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1983-61486K [26]

AB Protease producing mutant forms of the wild fungus, strain *Aspergillus niger* var. *tienhem* CBS 319.81, is claimed and comprises *A. niger* AP 114-III-69 (CBS 320.81), AP 114-IV-70 (CBS 321.81), AP 114-IV-74 (CBS 322.81) and AP 114-IV-80 (CBS 323.81). The wild strain is mutated by UV and is selected by spreading on a caseinate agar plate, adding a carboxyl protease-inhibitor (preferably pepstatin), incubating for a few days and isolating colonies obtained with intensified caseinolytic aura formation. These mutants are then grown in a nutrient medium containing assimilable C- and N-sources at pH 3-7 and 25-50 deg, preferably 27-32 deg. This can be used in the preparation of acid stable protease, having a broad activity spectrum, in high yields and on an industrial scale. (15pp)

L4 ANSWER 21 OF 44 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 86099024 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3909669
TITLE: [Protease inhibitors, serum endotoxin and serum immunoglobulins following portacaval end-to-side anastomosis in animal experiments].
Proteaseninhibitoren, Serum-Endotoxin und Serum-Immunglobuline nach portokavalier End-zu-Seit-Anastomose im Tierexperiment.
AUTHOR: Machraoui A; Rasche B; Oellig W P; Thiel H
SOURCE: Zeitschrift fur Gastroenterologie, (1985 Mar) Vol. 23, No. 3, pp. 130-8.
Journal code: 0033370. ISSN: 0044-2771.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990

Entered Medline: 31 Jan 1986

AB In order to clarify the pathophysiological mechanism of certain biochemical and immunological changes (endotoxin in serum, protease inhibitors, immunoglobulins) found in a former study on human cirrhosis of the liver the porto-caval end-to-side anastomosis of rats with unaffected livers was chosen as test model. With the aid of this bypass the "spill-over" phenomenon of the liver can be completely imitated. In this study, 7 operated and 5 or 14 control animals resp. are referred to. Serum endotoxin, acid-stable and acid-unstable protease inhibitors and immunoglobulins IgG, IgA and IgM were determined 20 months after operation. For the determination of potential hemodynamically or toxically induced effects on these organs, morphologic liver and lung examinations were performed. On the average, the operated rats showed a weight loss of 8 percent, i.e. from 378.4 +/- 9.2 g to 348.4 +/- 17 g. Compared to control rats, their relative liver weights were significantly lower (34%) (mean = 2.23 +/- 0.2 compared to 3.4 +/- 0.44 g, p less than 0.0005). Serum immunoglobulins IgG, IgA and IgM in operated animals were significantly higher (p less than 0.005 or p less than 0.025 resp. and 0.0025). Endotoxin in serum could be identified in 4 out of 7 operated animals (57, 1%), but in none of the control animals. While there was no difference in serum levels of acid-unstable protease inhibitors between the two groups levels of acid-stable protease inhibitors were in operated animals by 24% higher than in control animals (mean = 35.3 +/- 3.3 compared to 28.5 +/- 2.3 mU/ml, p less than 0.0005). (ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 22 OF 44 LIFESCI COPYRIGHT 2007 CSA on STN

ACCESSION NUMBER: 85:5762 LIFESCI

TITLE: Acid stable protease from mutants of genus *Aspergillus*.

AUTHOR: Bartnik, F.; Schindler, J.; Weiss, A.; Schmid, R.

CORPORATE SOURCE: Henkel Kommanditgesellschaft auf Aktien., Duesseldorf (FRG)

PATENT INFO.: US 4518697 1985

SOURCE: (1985) . US Cl. 435/254; Int. Cl. C12N 1/14, C12N 9/62, C12R 1/685..

DOCUMENT TYPE: Patent

FILE SEGMENT: A; W

LANGUAGE: English

AB This patent describes a mutant of *Aspergillus niger* CBS 319.81 selected for proteinase production.

L4 ANSWER 23 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1985-00497 BIOTECHDS

TITLE: Acid-stable protease from mutants of the genus *Rhizopus*; *Rhizopus rhizopodiformus* mutagenesis

PATENT ASSIGNEE: Henkel

PATENT INFO: US 4473644 25 Sep 1984

APPLICATION INFO: US 1982-409122 18 Aug 1982

PRIORITY INFO: DE 1981-132936 20 Aug 1981

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1983-22948K [10]

AB A process for the preparation of acid-stable protease having a broad activity spectrum is described. The protease is produced by cultivating mutant strains *Rhizopus rhizopodiformus* III-34 (CBS 219.80), III-46 (CBS 220.80), III-59 (CBS 221.80) and III-65 (CBS 222.80), having a greater protease-producing ability than the parent strain, in a culture medium containing assimilable C- and N-sources at pH 3-7 and at 25-50 deg, and separating the desired protease in a conventional manner. The mutants are preferably obtained by UV irradiation and have a proteolytic activity greater than 10, and especially 21 mTU/ml in agitated culture. The mutants are obtained by exposing spores to UV light until a high killing

rate of the spores is obtained, and the spores are then cultured on a nutrient medium containing casein. Colonies with caseinolytic activity are isolated and separately cultivated in agitated nutrient media to obtain the desired strains. High yields of acid-stable protease are obtained and the cultivation process can be repeated several times. (5pp)

L4 ANSWER 24 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1985:115373 BIOSIS
DOCUMENT NUMBER: PREV198529005369; BR29:5369
TITLE: IMMUNOLOGICAL AND ENZYMOLOGICAL STUDIES OF ACID STABLE PROTEASE INHIBITOR IN ASCITES OF OVARIAN CARCINOMA.
AUTHOR(S): AKAZAWA K [Reprint author]
CORPORATE SOURCE: 2ND DEP PHYSIOL, MIYAZAKI MED COLL, MIYAZAKI
SOURCE: Acta Obstetrica et Gynaecologica Japonica (Japanese Edition), (1984) Vol. 36, No. 11, pp. 2407.
Meeting Info.: 36TH ANNUAL SCIENTIFIC MEETING OF THE JAPAN SOCIETY OF OBSTETRICS AND GYNECOLOGY, SENDAI, JAPAN, MAY 13-16, 1984. ACTA OBSTET GYNAECOL JPN (JPN ED).
CODEN: NISFAY. ISSN: 0300-9165.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L4 ANSWER 25 OF 44 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 85002329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6434208
TITLE: Further purification and characterization of acid -stable protease inhibitor from ascites of an ovarian carcinoma patient.
AUTHOR: Akazawa K; Sumi H; Maruyama M; Mihara H
SOURCE: Clinica chimica acta; international journal of clinical chemistry, (1984 Sep 15) Vol. 142, No. 1, pp. 47-60.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198411
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 20 Nov 1984

AB An acid-stable protease inhibitor (AS-PI) has been previously demonstrated in ascitic fluid from patients with ovarian carcinoma. In this study, the AS-PI was further purified using DEAE-cellulose and isoelectric focusing (IEF), and a partial characterization was undertaken. On DEAE-cellulose ion-exchange column chromatography, AS-PI activity was observed in both adsorbed and non-adsorbed fractions. The former represented the main AS-PI peak. By IEF, the respective pI values were 1.6 and 4.5. By gel filtration, the molecular weight of the main (adsorbed fraction) AS-PI was 78 000. This AS-PI strongly inhibited trypsin and to a lesser extent chymotrypsin, but exerted no inhibitory effect on plasmin. It slightly inhibited SH proteases such as papain and ficin. Immunologically, AS-PI was distinct from alpha 1-antitrypsin, alpha 1-antichymotrypsin, inter-alpha-trypsin inhibitor, antithrombin III, C1-inactivator, alpha 2-macroglobulin and alpha 2-plasmin inhibitor. The main AS-PI reacted with and was neutralized by antiurinary trypsin inhibitor serum, and on immunoelectrophoresis, had a mobility slightly cathodal to serum albumin.

L4 ANSWER 26 OF 44 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1984-04492 BIOTECHDS

TITLE: Nutrient medium for growing yeasts and molds;
contains a dry hydrolysate mixture of skimmed milk and
cheese whey agar-agar bromophenol-blue and phosphate(s)

PATENT ASSIGNEE: N.Kavkaz-Inst.Oil-Petrol.Ind.

PATENT INFO: SU 1013469 23 Apr 1983

APPLICATION INFO: SU 1981-368455 30 Dec 1981

PRIORITY INFO: SU 1981-368455 30 Dec 1981

DOCUMENT TYPE: Patent

LANGUAGE: Russian

OTHER SOURCE: WPI: 1984-060715 [10]

AB A nutrient medium for yeasts and molds consists of a dry hydrolysate mixture of skimmed milk and cheese whey (I), agar-agar, bromophenol-blue, KH_2PO_4 and Na_2HPO_4 . (I) is obtained from a mixture of 68-70% skimmed milk of titratable acidity 90-100 deg T and 30-32% cheese whey. The mixture is hydrolyzed with a rennine-puzillin enzyme containing acid-resistant protease, at pH 4.8-5.4 and 6.0-6.5% reducible sugars, chloroform being added to the hydrolysis mixture 0.5-0.75 hr after the enzyme. The product is then dried. The resulting medium has good differentiation and growth properties and is of a low cost. Skimmed milk and cheese whey are heated together to 60 deg and powdered rennin-puzillin is added. Chloroform is added after 0.75 hr and the hydrolysate recovered after 5 hr contains 80 mg.% amino N and 4.2% reducible sugars. It is autoclaved, evaporated and spray-dried before mixing with agar-agar, bromophenol, KH_2PO_4 and Na_2HPO_4 . (5pp)

L4 ANSWER 27 OF 44 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 83285871 MEDLINE

DOCUMENT NUMBER: PubMed ID: 6411386

TITLE: Acid stable protease
inhibitor in ascites of ovarian carcinoma.

AUTHOR: Akazawa K; Sumi H; Maruyama M; Mihara H

SOURCE: Clinica chimica acta; international journal of clinical
chemistry, (1983 Jun 30) Vol. 131, No. 1-2, pp. 87-99.
Journal code: 1302422. ISSN: 0009-8981.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198310

ENTRY DATE: Entered STN: 19 Mar 1990

Last Updated on STN: 19 Mar 1990

Entered Medline: 8 Oct 1983

AB In patients with ovarian tumors, a novel protease inhibitor which is very stable in acid (AS-PI, acid stable protease inhibitor) was identified in the ascites and tumor fluid as well as in the urine and plasma. The highest AS-PI activity was observed in the tumor fluid of ovarian carcinomas (10.7 +/- 2.3 U/ml), followed by the ascites of ovarian carcinomas (8.2 +/- 4.2 U/ml). There was a significant difference in activity of the tumor fluid and ascites between malignant and benign tumors (p less than 0.005, p less than 0.05, respectively). The same antigenicity of AS-PI fractionated from ascites of ovarian carcinomas to urinary trypsin inhibitor was identified by double immunodiffusion and neutralization techniques. It migrated in the serum albumin fraction on immunoelectrophoresis. By gel filtration, the AS-PI in the ascites of ovarian carcinomas showed a molecular weight of 70000-80000. Two active components with molecular weights of 61300 +/- 2100 and 73300 +/- 2500 were detected by SDS polyacrylamide gel electrophoresis.

L4 ANSWER 28 OF 44 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 82229471 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7046595

TITLE: Distribution of antileukoprotease in upper respiratory mucosa.
 AUTHOR: Fryksmark U; Ohlsson K; Polling A; Tegner H
 SOURCE: The Annals of otology, rhinology, and laryngology, (1982 May-Jun) Vol. 91, No. 3 Pt 1, pp. 268-71.
 Journal code: 0407300. ISSN: 0003-4894.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 198208
 ENTRY DATE: Entered STN: 17 Mar 1990
 Last Updated on STN: 17 Mar 1990
 Entered Medline: 14 Aug 1982

AB Human respiratory tract secretions contain enzyme inhibitors derived from plasma and a low molecular weight, acid-stable protease inhibitor, antileukoprotease. The distribution of antileukoprotease in normal upper respiratory tract mucosa has been studied using an immunohistologic technique. The inhibitor was localized to the serous parts of the submucosal glands of the maxillary sinus and the trachea but was not demonstrable in mucous glands and goblet cells. It is concluded that the antileukoprotease found in respiratory tract secretions is produced locally in the submucosal serous glands.

L4 ANSWER 29 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN.
 ACCESSION NUMBER: 1982:96249 BIOSIS
 DOCUMENT NUMBER: PREV198223026241; BR23:26241
 TITLE: IMMUNOLOGICAL AND ENZYMOLOGICAL STUDIES ON ACID STABLE PROTEASE INHIBITOR IN ASCITES OF OVARIAN CANCER.
 AUTHOR(S): AKAZAWA K [Reprint author]
 CORPORATE SOURCE: DEP OBSTET GYNECOL, MIYAZAKI MED COLLEGE, MIYAZAKI
 SOURCE: Acta Obstetrica et Gynaecologica Japonica (Japanese Edition), (1981) Vol. 33, No. 12, pp. 2250-2251.
 Meeting Info.: 33RD ANNUAL SCIENTIFIC MEETING OF THE JAPAN SOCIETY OF OBSTETRICS AND GYNECOLOGY, NIIGATA, JAPAN, MAY 10-13, 1981. ACTA OBSTET GYNAECOL JPN.
 CODEN: NISFAY. ISSN: 0300-9165.
 DOCUMENT TYPE: Conference; (Meeting)
 FILE SEGMENT: BR
 LANGUAGE: ENGLISH

L4 ANSWER 30 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 12
 ACCESSION NUMBER: 1979:3460 BIOSIS
 DOCUMENT NUMBER: PREV197916003460; BR16:3460
 TITLE: ACID STABLE PROTEASE INHIBITORS IN HUMAN AND RHESUS MONKEY SPERM PLASMA.
 AUTHOR(S): SCHIESSLER H; ARNHOLD M
 SOURCE: Biology of Reproduction, (1978) Vol. 18, No. SUPPL 1, pp. 77A.
 CODEN: BIREBV. ISSN: 0006-3363.
 DOCUMENT TYPE: Article
 FILE SEGMENT: BR
 LANGUAGE: Unavailable

L4 ANSWER 31 OF 44 MEDLINE on STN
 DUPLICATE 13
 ACCESSION NUMBER: 77226509 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 881164
 TITLE: Isolation and partial characterization of a low molecular weight acid stable protease inhibitor from human bronchial secretion.

AUTHOR: Ohlsson K; Tegner H; Akesson U
SOURCE: Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1977
May) Vol. 358, No. 5, pp. 583-9.
Journal code: 2985060R. ISSN: 0018-4888.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197709
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 17 Sep 1977

AB An acid stable protease inhibitor was isolated from human bronchial secretion. Two important stages of the purification procedure were affinity chromatography on trypsin bound to Affi-Gel 10 and ion-exchange chromatography on SP-Sephadex C-50. The isolated inhibitor appeared as a single band on analytical disc electrophoresis and eluted as a homogeneous protein peak on gel filtration on Sephadex G-75 corresponding to a molecular weight of about 10500. Amino acid analyses showed no tryptophan or histidine and as N-terminal amino acid tyrosine. No glucosamine or galactosamine was detected. The results of the analyses suggest that the purified inhibitor is identical to the low molecular weight trypsin-chymotrypsin inhibitor of human seminal plasma (HUSI-I).

L4 ANSWER 32 OF 44 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 14

ACCESSION NUMBER: 78186764 EMBASE
DOCUMENT NUMBER: 1978186764
TITLE: Specific degradation of histones H1 and H3.
AUTHOR: Fornells M.; Subirana J.A.
CORPORATE SOURCE: Dept. Quim. Macromolec., CSIC, Esc. T.S. Ing. Industr.,
Barcelona, Spain
SOURCE: Biochemical and Biophysical Research Communications, (1977)
Vol. 78, No. 1, pp. 217-221.
CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

AB It is shown that acid treated histones H1 and H3 are susceptible to specific degradation by an associated acid resistant protease. Dialysis against distilled water (pH 5.5-6) of the acid treated histones enhances proteolysis. On the other hand, no degradation is observed in nucleohistone either in the presence of Ca++ or Na++ ions. The conditions required to avoid degradation during nucleohistone and histone manipulation are described.

L4 ANSWER 33 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1976:507091 HCAPLUS
DOCUMENT NUMBER: 85:107091
TITLE: The level of acid stable
protease inhibitors in plasma as an indicator
of renal function
AUTHOR(S): Feuth, H.; Kemkes, B. M.; Hochstrasser, K.
CORPORATE SOURCE: Biochem. Lab., Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Protides of the Biological Fluids (1976), Volume Date
1975, 23, 445-9
CODEN: PBFP66; ISSN: 0079-7065
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 12 refs. of protease inhibitors of plasma and urine in normal subjects and in patients with various nephropathies.

L4 ANSWER 34 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1975:230524 BIOSIS
DOCUMENT NUMBER: PREV197560060520; BA60:60520
TITLE: SCREENING SOME SOIL FUNGI FOR PRODUCTION OF ACID STABLE PROTEASES.
AUTHOR(S): VASANTHA M B; GOPALKRISHNAN K S
SOURCE: Maharashtra Vidnyan Mandir Patrika, (1974) Vol. 9, No. 1-2, pp. 16-21.
CODEN: MVMPAC. ISSN: 0374-941X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

L4 ANSWER 35 OF 44 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 75059163 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4548039
TITLE: [Characterization of the acid-stable protease inhibitors in human plasma (author's transl)].
Zur Charakterisierung der surestabilen Proteaseninhibitoren aus Humanplasma.
AUTHOR: Hochstrasser K; Feuth H; Steiner O
SOURCE: Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1973 Aug) Vol. 354, No. 8, pp. 927-32.
Journal code: 2985060R. ISSN: 0018-4888.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 18 Mar 1975

L4 ANSWER 36 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1973:490458 HCAPLUS
DOCUMENT NUMBER: 79:90458
TITLE: Antigenic relation between the human bronchial mucus inhibitor and plasma inter- α -trypsin inhibitor
AUTHOR(S): Hochstrasser, Karl; Reichert, Ruediger; Heimbürger, Norbert
CORPORATE SOURCE: Hals-, Nasen-, Ohren-Klin., Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1973), 354(5), 587-8
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The low-mol.-weight and acid-stable protease inhibitor of human bronchial mucus gave an immunopptn. with antiserum against the inter- α -trypsin inhibitor of plasma. The inhibitors differed in the mol. weight and in the electrophoretic mobility. Both inhibitors were arginine inhibitors and seem to have the same antigenic determinants and the same reactive sites.

L4 ANSWER 37 OF 44 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 74050425 EMBASE
DOCUMENT NUMBER: 1974050425
TITLE: [Identification of a low molecular protease inhibitor in the mucous membranes of the respiratory tract].
DER NACHWEIS EINES NIEDERMOLEKULAREN PROTEASENINHIBITORS IN

SCHLEIMHAUTEN DER ATEMWEGE.
AUTHOR: Reichert R.; Hochstrasser K.; Elgas W.
CORPORATE SOURCE: Biochem. Lab., HNO Univ. Klin., Munchen, Germany
SOURCE: MSCHR.OHRENHEILK., (1973) Vol. 107, No. 7, pp. 331-334. .
CODEN: MOLAAF
DOCUMENT TYPE: Journal
FILE SEGMENT: 011 Otorhinolaryngology
029 Clinical Biochemistry
LANGUAGE: German

AB The nasal and bronchial mucus contains a low molecular acid stable protease inhibitor, which inhibits the hydrolytic enzymes trypsin and chymotrypsin as well as the proteolytic enzymes of leukocytes. It seems to be the physiological sense of this protease inhibitor to inhibit these enzymes which occur during infections out of disintegrated leucocytes. The protease inhibitor is a product of the mucous membranes of the respiratory tract. Thus the inhibitor can be determined in the ciliated epithelium itself. The content of this protease inhibitor was found to be high in the nasal and tracheal mucous membranes; lower degrees were found in the paranasal sinus.

L4 ANSWER 38 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:512514 HCAPLUS
DOCUMENT NUMBER: 77:112514
TITLE: Acid-stable and thermostable protease
INVENTOR(S): Yokotsuka, Tamotsu; Hashimoto, Hikotaka; Iwasa, Takashi
PATENT ASSIGNEE(S): Kikkoman Shoyu Co., Ltd.
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 3674644 | A | 19720704 | US 1969-884740 | 19691212 |
| JP 49024670 | B | 19740625 | JP 1969-79624 | 19691007 |
| PRIORITY APPLN. INFO.: | | | JP 1968-95002 | A 19681226 |
| | | | JP 1969-79624 | A 19691007 |

AB Penicillium duponti ATCC 20186 produced a new acid-stable and thermostable protease. Thus, P. duponti was cultured in a solid medium at 40° for 4 days. The protease was extracted from the medium and added to a substrate of defatted soybean. The optimum enzymic activity is at pH 2.0-3.0. The protease can work in a temperature range from room temperature to 90°. The optimum temperature is 60° at pH 2.5, 75° at pH 3.5, and 75°-80° at a pH of 4.5 with a slight liberation of amino acids.

L4 ANSWER 39 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:103741 HCAPLUS
DOCUMENT NUMBER: 76:103741
TITLE: Antiinflammatory enzymic preparation
INVENTOR(S): Koaze, Yoshihisa; Ueta, Masahiro; Kuroda, Michio; Koeda, Takemi; Shibata, Yuichi
PATENT ASSIGNEE(S): Meiji Confectionary Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 3 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

JP 46042595 B4 19711216 JP 19680605
AB Acid-resistant protease (I) of *Aspergillus niger* macrosporus was aged with pancreatin (II) in aqueous media at 10-50° and pH 2.5-7.0 to raise the antiinflammatory activity against carrageenin edema. Thus, 12.5 g I and 2.5 g II in 150 ml buffer (pH 4) was kept at 37° for 72 hr, fractionated with Sephadex G 50, and freeze-dried.

L4 ANSWER 40 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:146263 HCAPLUS
DOCUMENT NUMBER: 74:146263
TITLE: Cosmetics containing acid-resistant protease for skin
INVENTOR(S): Ozaki, Yoshihisa; Goi, Hitoshi
PATENT ASSIGNEE(S): Meiji Confectionary Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 4 pp.
 CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| | JP 45028918 | B4 | 19700921 | JP | 19650628 |
| AB | Milk caseins, egg albumins, gelatins, casamino acids, methionine, soluble starches, dextrin, galactose, ascorbic acid, and Mn sulfate are used as stabilizers. | | | | |

L4 ANSWER 41 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:4626 HCAPLUS
DOCUMENT NUMBER: 62:4626
ORIGINAL REFERENCE NO.: 62:885f-g
TITLE: Digestive enzymes. XLIX. Acid-fast protease produced by *Aspergillus niger*
AUTHOR(S): Okazaki, Kanzo; Eda, Hiroko
CORPORATE SOURCE: Tohoku Univ., Sendai, Japan
SOURCE: Yakuzaigaku (1964), 24, 133-6
 CODEN: YAKUA2; ISSN: 0372-7629
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 61, 11186c. An acid-stable protease preparation produced from *Aspergillus niger* was studied. The optimal pH was 2.5-3.0 and the activity was not decreased at pH 1.8 for 2 hrs. In a stomach model, the best results were obtained at pH 3-4.

L4 ANSWER 42 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:406072 HCAPLUS
DOCUMENT NUMBER: 61:6072
ORIGINAL REFERENCE NO.: 61:999e-f
TITLE: Acid-stable hydrolytic enzyme. VI. Protease and amylase of *Paecilomyces varioti* TPR-220
AUTHOR(S): Misiaki, Tetsuo; Yasui, Hajime; Sawada, Jiro; Tanaka, Ichiro
CORPORATE SOURCE: Taisho Pharm. Co., Ltd., Tokyo
SOURCE: Nippon Nogei Kagaku Kaishi (1961), 35, 1264-70
 CODEN: NNKKAA; ISSN: 0002-1407
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A newly isolated strain TPR-220, which produced a high amount of acid-stable protease, was determined to belong to *P. varioti*. Enzyme solns. of TPR-220 extracted from wheat bran contained a stronger acid-protease (at pH 3) than those of *A. saitoi* and TPR-18, but

the activity of neutral protease was weaker than that of TPR-18. The dextrinogenic amylase produced by TPR220 was stable to acid treatment at pH 3 for 30 min. at 30°. The enzyme activities of the strains irradiated with ultraviolet ray were .apprx.90% of the original activity of the parent strain.

L4 ANSWER 43 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1962:67206 HCAPLUS
DOCUMENT NUMBER: 56:67206
ORIGINAL REFERENCE NO.: 56:13015c-d
TITLE: Digestive drugs. XXIV. Acid-resistant protease produced from *Aspergillus saitoi*
AUTHOR(S): Okazaki, Kanzo; Hata, Kofuji; Komatsu, Haruko
CORPORATE SOURCE: Tohoku Univ., Sendai
SOURCE: Yakuzaigaku (1960), 20, 272-8
CODEN: YAKUA2; ISSN: 0372-7629
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Proteolytic enzyme preparation (I), produced from *A. saitoi*, is for use as a digestive and the optimal pH for the proteolytic action is 2.7-3.0. I is resistant to HCl in the region of pH 2.0 but is inactivated in alkaline solution

It is not desirable to combine I with antacids, but to administer I in acid solution with 0.5% citric or tartaric acid, because I has a very acidic optimal pH and is stable in such acid solns.

L4 ANSWER 44 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1958:3362 HCAPLUS
DOCUMENT NUMBER: 52:3362
ORIGINAL REFERENCE NO.: 52:651a-b
TITLE: Protein turbidity of sake. III. Formation of flocculating enzyme in surface culture by *Aspergillus oryzae*
AUTHOR(S): Akiyama, Hiroichi; Fujii, Ryuji; Harada, Masayuki
CORPORATE SOURCE: Tax Admin. Agency, Tokyo
SOURCE: Nippon Jozo Kyokai Zasshi (1957), 52, 226-31
CODEN: NIJKA4; ISSN: 0369-416X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Sources of N in the medium have a critical role for the formation of the flocculating enzyme. Protein N sources all are very effective. Of the amino acids tested, leucine, isoleucine, methionine, phenylalanine, and tryptophan were effective to the same degree as protein N sources; tyrosine, threonine, arginine, and valine also were effective but to lower degree; and the other amino acids, i.e., glycine, alanine, glutamic acid, aspartic acid, Na glutamate, proline, hydroxyproline, histidine, lysine, and cystine, and inorg. N sources were ineffective. Final pH of the medium was best at 3.5 for the yield of enzyme. The enzyme was shown to be a new enzyme belonging to the acid-stable proteases and its optimum pH was at about pH 4.0.

=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

L1 21366 S ACID (W) (RESISTANT OR STABLE)
L2 515920 S PROTEASE?
L3 85 S L1(W)L2
L4 44 DUP REM L3 (41 DUPLICATES REMOVED)

=> s (cereal or nutri? or (protein (w)source)) and l4
L5 6 (CEREAL OR NUTRI? OR (PROTEIN (W) SOURCE)) AND L4

=> d 1-6 ibib ab

L5 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:1742 BIOSIS
DOCUMENT NUMBER: PREV200500011483
TITLE: Dietary supplements containing natural ingredients.
AUTHOR(S): Perkes, Lynn [Inventor, Reprint Author]
CORPORATE SOURCE: ASSIGNEE: Melaleuca, Inc.
PATENT INFORMATION: US 6818233 20041116
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (Nov 16 2004) Vol. 1288, No. 3.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004

AB The invention provides a dietary supplement comprising at least one
flavonoid source and an enzyme, that is effective for inhibiting in vivo
platelet activity and LDL cholesterol oxidation in a mammal at a dosage of
about 30 mg/Kg or less. The supplement may contain flavonoid sources
found in grape seed extracts, grape skin extracts, bilberry extracts,
ginkgo biloba extracts or the flavonoid quercetin. The supplement may
also contain fungal proteases, acid stable
proteases and bromelain. The invention further provides a method
for using the dietary supplement and an article of manufacture containing
the supplement.

L5 ANSWER 2 OF 6 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-16039 BIOTECHDS
TITLE: Use of acid stable protease for
producing a food composition;
for use as feedstuff, as a food-additive and in vegetable
protein treatment
AUTHOR: Oestergaard P R; Sjoeholm C
PATENT ASSIGNEE: Roche
LOCATION: Basle, Switzerland.
PATENT INFO: WO 2001058276 16 Aug 2001
APPLICATION INFO: WO 2001-EP1153 5 Feb 2001
PRIORITY INFO: DK 2000-200 8 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-488930 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where
the protease has identity of at least 70% to a 188 amino acid sequence
(I) and or a 17 amino acid sequence (II), is claimed. Also claimed are:
improving the nutritional value of feedstuff; an animal
food-additive; and treatment of vegetable proteins. At least one
acid stable protease is useful in the
preparation of a composition for use in feedstuff. The protease has 71%
identity to (I) and/or (II). The dosage of the protease is 0.01-200 mg.
The feed composition is useful for feeding animals, including humans.
Animals include ruminants and non-ruminants i.e. monogastric animals
i.e. pigs, poultry and fish. The feedstuff comprises phytase,
endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase
(EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable
source. (49pp)

L5 ANSWER 3 OF 6 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-16038 BIOTECHDS
TITLE: Use of acid stable protease of

the subtilisin for producing a food composition;
for use as feedstuff, as a food-additive and in vegetable
protein treatment

AUTHOR: Oestergaard P R; Sjoeholm C; Klunter A
PATENT ASSIGNEE: Roche
LOCATION: Basle, Switzerland.
PATENT INFO: WO 2001058275 16 Aug 2001
APPLICATION INFO: WO 2001-EP1152 5 Feb 2001
PRIORITY INFO: DK 2000-200 8 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-488929 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where the protease is of the subtilisin family and/or has less than 10% residual activity when inhibited with subtilisin, is claimed. Also claimed are: improving the nutritional value of feedstuff; an animal food-additive; and treatment of vegetable proteins. At least one acid stable protease is useful in the preparation of a composition for use in feedstuff. The protease is of the subtilisin family and/or 10% residual activity when inhibited with subtilisin. The dosage of the protease is 0.01-200 mg/kg of feed. The feed composition is useful for feeding animals, including humans. Animals include ruminants and non-ruminants i.e. monogastric animals i.e. pigs, poultry and fish. The feedstuff comprises phytase, endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase (EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable source. (63pp)

L5 ANSWER 4 OF 6 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1985-08801 BIOTECHDS

TITLE: Acid stable protease from
mutants of *Aspergillus niger*;
mutagenesis of the wild strain

PATENT ASSIGNEE: Henkel
PATENT INFO: US 4518697 21 May 1985
APPLICATION INFO: US 1982-449415 13 Dec 1982
PRIORITY INFO: DE 1981-149457 14 Dec 1981
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1983-61486K [26]

AB Protease producing mutant forms of the wild fungus, strain *Aspergillus niger* var. *tienhem* CBS 319.81, is claimed and comprises A. *niger* AP 114-III-69 (CBS 320.81), AP 114-IV-70 (CBS 321.81), AP 114-IV-74 (CBS 322.81) and AP 114-IV-80 (CBS 323.81). The wild strain is mutated by UV and is selected by spreading on a caseinate agar plate, adding a carboxyl protease-inhibitor (preferably pepstatin), incubating for a few days and isolating colonies obtained with intensified caseinolytic aura formation. These mutants are then grown in a nutrient medium containing assimilable C- and N-sources at pH 3-7 and 25-50 deg, preferably 27-32 deg. This can be used in the preparation of acid stable protease, having a broad activity spectrum, in high yields and on an industrial scale. (15pp)

L5 ANSWER 5 OF 6 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1985-00497 BIOTECHDS

TITLE: Acid-stable protease from
mutants of the genus *Rhizopus*;
Rhizopus rhizopodiformis mutagenesis

PATENT ASSIGNEE: Henkel
PATENT INFO: US 4473644 25 Sep 1984
APPLICATION INFO: US 1982-409122 18 Aug 1982
PRIORITY INFO: DE 1981-132936 20 Aug 1981
DOCUMENT TYPE: Patent
LANGUAGE: English

OTHER SOURCE: WPI: 1983-22948K [10]

AB A process for the preparation of acid-stable protease having a broad activity spectrum is described. The protease is produced by cultivating mutant strains *Rhizopus rhizopodiformus* III-34 (CBS 219.80), III-46 (CBS 220.80), III-59 (CBS 221.80) and III-65 (CBS 222.80), having a greater protease-producing ability than the parent strain, in a culture medium containing assimilable C- and N-sources at pH 3-7 and at 25-50 deg, and separating the desired protease in a conventional manner. The mutants are preferably obtained by UV irradiation and have a proteolytic activity greater than 10, and especially 21 mTU/ml in agitated culture. The mutants are obtained by exposing spores to UV light until a high killing rate of the spores is obtained, and the spores are then cultured on a nutrient medium containing casein. Colonies with caseinolytic activity are isolated and separately cultivated in agitated nutrient media to obtain the desired strains. High yields of acid-stable protease are obtained and the cultivation process can be repeated several times. (5pp)

L5 ANSWER 6 OF 6 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 1984-04492 BIOTECHDS

TITLE: Nutrient medium for growing yeasts and molds;
contains a dry hydrolysate mixture of skimmed milk and cheese whey agar-agar bromophenol-blue and phosphate(s)

PATENT ASSIGNEE: N.Kavkaz-Inst.Oil-Petrol.Ind.

PATENT INFO: SU 1013469 23 Apr 1983

APPLICATION INFO: SU 1981-368455 30 Dec 1981

PRIORITY INFO: SU 1981-368455 30 Dec 1981

DOCUMENT TYPE: Patent

LANGUAGE: Russian

OTHER SOURCE: WPI: 1984-060715 [10]

AB A nutrient medium for yeasts and molds consists of a dry hydrolysate mixture of skimmed milk and cheese whey (I), agar-agar, bromophenol-blue, KH_2PO_4 and Na_2HPO_4 . (I) is obtained from a mixture of 68-70% skimmed milk of titratable acidity 90-100 deg T and 30-32% cheese whey. The mixture is hydrolyzed with a rennine-puzillin enzyme containing acid-resistant protease, at pH 4.8-5.4 and 6.0-6.5% reducible sugars, chloroform being added to the hydrolysis mixture 0.5-0.75 hr after the enzyme. The product is then dried. The resulting medium has good differentiation and growth properties and is of a low cost. Skimmed milk and cheese whey are heated together to 60 deg and powdered rennin-puzillin is added. Chloroform is added after 0.75 hr and the hydrolysate recovered after 5 hr contains 80 mg.% amino N and 4.2% reducible sugars. It is autoclaved, evaporated and spray-dried before mixing with agar-agar, bromophenol, KH_2PO_4 and Na_2HPO_4 . (5pp)

=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

L1 21366 S ACID (W) (RESISTANT OR STABLE)

L2 515920 S PROTEASE?

L3 85 S L1(W)L2

L4 44 DUP REM L3 (41 DUPLICATES REMOVED)

L5 6 S (CEREAL OR NUTRI? OR (PROTEIN (W)SOURCE)) AND L4

=> s nocardiosis###

L6 1048 NOCARDIOPSIS###

=> s l2 and l6

L7 130 L2 AND L6

=> s 11 and 17

L8 8 L1 AND L7

=> dup rem 18

PROCESSING COMPLETED FOR L8

L9 4 DUP REM L8 (4 DUPLICATES REMOVED)

=> d 1-4 ibib ab

L9 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2007212629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17382344
TITLE: Structural and mechanistic exploration of acid resistance:
kinetic stability facilitates evolution of extremophilic
behavior.
AUTHOR: Kelch Brian A; Eagen Kyle P; Erciyas F Pinar; Humphris
Elisabeth L; Thomason Adam R; Mitsuiki Shinji; Agard David
A
CORPORATE SOURCE: Howard Hughes Medical Institute and the Department of
Biochemistry and Biophysics, University of California-San
Francisco, 600 16th Street, San Francisco, CA 94158-2517,
USA.
SOURCE: Journal of molecular biology, (2007 May 4) Vol. 368, No. 3,
pp. 870-83. Electronic Publication: 2007-02-22.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-2OUA
ENTRY MONTH: 200708
ENTRY DATE: Entered STN: 10 Apr 2007
Last Updated on STN: 8 Aug 2007
Entered Medline: 7 Aug 2007
AB Kinetically stable proteins are unique in that their stability is
determined solely by kinetic barriers rather than by thermodynamic
equilibria. To better understand how kinetic stability promotes protein
survival under extreme environmental conditions, we analyzed the unfolding
behavior and determined the structure of *Nocardiopsis alba*
Protease A (NAPase), an acid-resistant,
kinetically stable protease, and compared these results with a
neutrophilic homolog, alpha-lytic protease (alphaLP). Although
NAPase and alphaLP have the same number of acid-titratable residues,
kinetic studies revealed that the height of the unfolding free energy
barrier for NAPase is less sensitive to acid than that of alphaLP, thereby
accounting for NAPase's improved tolerance of low pH. A comparison of the
alphaLP and NAPase structures identified multiple salt-bridges in the
domain interface of alphaLP that were relocated to outer regions of
NAPase, suggesting a novel mechanism of acid stability in which
acid-sensitive electrostatic interactions are rearranged to similarly
affect the energetics of both the native state and the unfolding
transition state. An acid-stable variant of alphaLP
in which a single interdomain salt-bridge is replaced with a corresponding
intradomain NAPase salt-bridge shows a dramatic >15-fold increase in acid
resistance, providing further evidence for this hypothesis. These
observations also led to a general model of the unfolding transition state
structure for alphaLP protease family members in which the two
domains separate from each other while remaining relatively intact
themselves. These results illustrate the remarkable utility of kinetic
stability as an evolutionary tool for developing longevity over a broad
range of harsh conditions.

L9 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2005:548417 BIOSIS
 DOCUMENT NUMBER: PREV200510345270
 TITLE: Use of acid-stable proteases
 in animal feed.
 AUTHOR(S): Sjoeholm, Carsten [Inventor]; Oestergaard, Peter Rahbek
 [Inventor]
 CORPORATE SOURCE: Alleroed, Denmark
 ASSIGNEE: F. Hoffman-La Roche AG
 PATENT INFORMATION: US 06855548 20050215
 SOURCE: Official Gazette of the United States Patent and Trademark
 Office Patents, (FEB 15 2005)
 CODEN: OGUPE7. ISSN: 0098-1133.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 ENTRY DATE: Entered STN: 7 Dec 2005
 Last Updated on STN: 7 Dec 2005

AB Acid-stable proteases homologous to those
 derived from strains of the genus Nocardiosis, their use in
 animal feed, feed-additives and feed compositions containing such
 proteases, and methods for the treatment of vegetable proteins
 using such proteases.

L9 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:1354631 HCAPLUS
 DOCUMENT NUMBER: 144:83055
 TITLE: Cloning, characterization and sequences of
 proteases from Nocardiosis, and
 their use in animal feed and detergents
 INVENTOR(S): Lassen, Soeren Flensted; Sjoeholm, Carsten;
 Oestergaard, Peter Rahbek; Fischer, Morten
 PATENT ASSIGNEE(S): Novozymes A/S, Den.
 SOURCE: PCT Int. Appl., 90 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2005123911 | A2 | 20051229 | WO 2005-DK396 | 20050617 |
| WO 2005123911 | A3 | 20060209 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2005254611 | A1 | 20051229 | AU 2005-254611 | 20050617 |
| EP 1766001 | A2 | 20070328 | EP 2005-748647 | 20050617 |
| R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| IN 2006CN04687 | A | 20070629 | IN 2006-CN4687 | 20061221 |
| PRIORITY APPLN. INFO.: | | | DK 2004-969 | A 20040621 |
| | | | WO 2005-DK396 | W 20050617 |

AB The present invention relates to proteases derived from
 Nocardiosis dassonvillei subsp. dassonvillei DSM43235,

Nocardiopsis prasina DSM15649, Nocardiopsis prasina (previously alba) DSM14010, Nocardiopsis sp. DSM16424, Nocardiopsis alkaliphila DSM44657 and Nocardiopsis lucentensis DSM44048, as well as homologous proteases; their recombinant production in various hosts, including transgenic plants and non-human animals, and their use in animal feed and detergents. Cloning, expression and purification of the proteases is reported, and the nucleotide sequences and the encoded amino acid sequences of the proteases are disclosed. The proteases are acid-stable, alkali-stable, and/or thermostable.

L9 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:597756 HCAPLUS

DOCUMENT NUMBER: 135:152030

TITLE: Use of acid-stable proteases in animal feed

INVENTOR(S): Oestergaard, Peter Rahbek; Sjoeholm, Carsten

PATENT ASSIGNEE(S): F Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|-------------|
| WO 2001058276 | A2 | 20010816 | WO 2001-EP1153 | 20010205 |
| WO 2001058276 | A3 | 20020221 | | |
| W: | | | | |
| AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: | | | | |
| GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2395343 | A1 | 20010816 | CA 2001-2395343 | 20010205 |
| EP 1257176 | A2 | 20021120 | EP 2001-915190 | 20010205 |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001008164 | A | 20030121 | BR 2001-8164 | 20010205 |
| JP 2003521908 | T | 20030722 | JP 2001-557400 | 20010205 |
| AU 781415 | B2 | 20050519 | AU 2001-42366 | 20010205 |
| EP 1642506 | A2 | 20060405 | EP 2005-108903 | 20010205 |
| EP 1642506 | A3 | 20070425 | | |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| US 2001026797 | A1 | 20011004 | US 2001-779323 | 20010208 |
| US 6855548 | B2 | 20050215 | | |
| US 2003021774 | A1 | 20030130 | US 2001-779334 | 20010208 |
| US 6960462 | B2 | 20051101 | | |
| TW 259759 | B | 20060811 | TW 2001-90115232 | 20010622 |
| MX 2002PA07613 | A | 20021213 | MX 2002-PA7613 | 20020807 |
| US 2004161448 | A1 | 20040819 | US 2003-713394 | 20031114 |
| US 2005148060 | A1 | 20050707 | US 2005-74491 | 20050308 |
| PRIORITY APPLN. INFO.: | | | DK 2000-200 | A 20000208 |
| | | | US 2000-183133P | P 20000217 |
| | | | EP 2001-907489 | A3 20010205 |
| | | | WO 2001-EP1153 | W 20010205 |
| | | | US 2001-779323 | A1 20010208 |
| | | | US 2001-779334 | A1 20010208 |

AB Disclosed are acid-stable proteases

homologous to those derived from strains of the genus Nocardiosis
, their use in animal feed, feed-additives and feed compns. containing such
proteases, and methods for the treatment of vegetable proteins
using such proteases.

=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

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L2      515920 S PROTEASE?
L3      85 S L1(W)L2
L4      44 DUP REM L3 (41 DUPLICATES REMOVED)
L5      6 S (CEREAL OR NUTRI? OR (PROTEIN (W)SOURCE)) AND L4
L6      1048 S NOCARDIOPSIS###
L7      130 S L2 AND L6
L8      8 S L1 AND L7
L9      4 DUP REM L8 (4 DUPLICATES REMOVED)
```

=> e sjoeholm c/au

```
E1      10      SJOEHOLM B/AU
E2      1      SJOEHOLM BIRGITTA/AU
E3      13 --> SJOEHOLM C/AU
E4      24      SJOEHOLM CARSTEN/AU
E5      2      SJOEHOLM ELISABETH/AU
E6      1      SJOEHOLM ELISABETH A/AU
E7      1      SJOEHOLM EVA/AU
E8      1      SJOEHOLM F/AU
E9      1      SJOEHOLM G/AU
E10     1      SJOEHOLM GOERAN HENRY/AU
E11     1      SJOEHOLM GOESTA/AU
E12     11     SJOEHOLM H/AU
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=> s e3-e4

```
L10     37 ("SJOEHOLM C"/AU OR "SJOEHOLM CARSTEN"/AU)
```

=> e oestergaard p r/au

```
E1      4      OESTERGAARD P AA/AU
E2      15     OESTERGAARD P B/AU
E3      9 --> OESTERGAARD P R/AU
E4      1      OESTERGAARD PEDERSEN L/AU
E5      1      OESTERGAARD PEDERSEN LARS/AU
E6      12     OESTERGAARD PER/AU
E7      10     OESTERGAARD PER B/AU
E8      1      OESTERGAARD PER BJOERN/AU
E9      15     OESTERGAARD PETER RAHBK/AU
E10     1      OESTERGAARD PREHEN/AU
E11     1      OESTERGAARD R V/AU
E12     34     OESTERGAARD S/AU
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=> s e3-e9

```
L11     49 ("OESTERGAARD P R"/AU OR "OESTERGAARD PEDERSEN L"/AU OR "OESTERG
AARD PEDERSEN LARS"/AU OR "OESTERGAARD PER"/AU OR "OESTERGAARD
PER B"/AU OR "OESTERGAARD PER BJOERN"/AU OR "OESTERGAARD PETER
RAHBK"/AU)
```

=> s l10 or l11

```
L12     76 L10 OR L11
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=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

L1 21366 S ACID (W) (RESISTANT OR STABLE)
L2 515920 S PROTEASE?
L3 85 S L1(W)L2
L4 44 DUP REM L3 (41 DUPLICATES REMOVED)
L5 6 S (CEREAL OR NUTRI? OR (PROTEIN (W)SOURCE)) AND L4
L6 1048 S NOCARDIOPSIS###
L7 130 S L2 AND L6
L8 8 S L1 AND L7
L9 4 DUP REM L8 (4 DUPLICATES REMOVED)
E SJOEHOLM C/AU
L10 37 S E3-E4
E OESTERGAARD P R/AU
L11 49 S E3-E9
L12 76 S L10 OR L11

=> s l3 and l12

L13 6 L3 AND L12

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 4 DUP REM L13 (2 DUPLICATES REMOVED)

=> d 1-4 ibib ab

L14 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:307362 BIOSIS
DOCUMENT NUMBER: PREV200600314107
TITLE: Use of acid-stable subtilisin proteases in animal feed.
AUTHOR(S): Sjoeholm, Carsten [Inventor]; Oestergaard,
Peter Rahbek [Inventor]; Klunter, Anna-Marie
[Inventor]
CORPORATE SOURCE: Allerod, Denmark
ASSIGNEE: DSM IP Assets B. V
PATENT INFORMATION: US 06960462 20051101
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (NOV 1 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2006
Last Updated on STN: 14 Jun 2006

AB Acid-stable proteases of the subtilisin
family, their use in animal feed, feed-additives and feed compositions
containing such proteases, and methods for the treatment of vegetable
proteins using such proteases.

L14 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:548417 BIOSIS
DOCUMENT NUMBER: PREV200510345270
TITLE: Use of acid-stable proteases
in animal feed.
AUTHOR(S): Sjoeholm, Carsten [Inventor]; Oestergaard,
Peter Rahbek [Inventor]
CORPORATE SOURCE: Allerod, Denmark
ASSIGNEE: F. Hoffman-La Roche AG
PATENT INFORMATION: US 06855548 20050215
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (FEB 15 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent

LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005

AB Acid-stable proteases homologous to those derived from strains of the genus Nocardioopsis, their use in animal feed, feed-additives and feed compositions containing such proteases, and methods for the treatment of vegetable proteins using such proteases.

L14 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1

ACCESSION NUMBER: 2001-16039 BIOTECHDS
TITLE: Use of acid stable protease for producing a food composition; for use as feedstuff, as a food-additive and in vegetable protein treatment

AUTHOR: Oestergaard P R; Sjoeholm C
PATENT ASSIGNEE: Roche
LOCATION: Basle, Switzerland.
PATENT INFO: WO 2001058276 16 Aug 2001
APPLICATION INFO: WO 2001-EP1153 5 Feb 2001
PRIORITY INFO: DK 2000-200 8 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-488930 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where the protease has identity of at least 70% to a 188 amino acid sequence (I) and or a 17 amino acid sequence (II), is claimed. Also claimed are: improving the nutritional value of feedstuff; an animal food-additive; and treatment of vegetable proteins. At least one acid stable protease is useful in the preparation of a composition for use in feedstuff. The protease has 71% identity to (I) and/or (II). The dosage of the protease is 0.01-200 mg. The feed composition is useful for feeding animals, including humans. Animals include ruminants and non-ruminants i.e. monogastric animals i.e. pigs, poultry and fish. The feedstuff comprises phytase, endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase (EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable source. (49pp)

L14 ANSWER 4 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 2

ACCESSION NUMBER: 2001-16038 BIOTECHDS
TITLE: Use of acid stable protease of the subtilisin for producing a food composition; for use as feedstuff, as a food-additive and in vegetable protein treatment

AUTHOR: Oestergaard P R; Sjoeholm C; Klunter A
PATENT ASSIGNEE: Roche
LOCATION: Basle, Switzerland.
PATENT INFO: WO 2001058275 16 Aug 2001
APPLICATION INFO: WO 2001-EP1152 5 Feb 2001
PRIORITY INFO: DK 2000-200 8 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-488929 [53]

AB The use of at least one stable protease (EC-3.4.21.62) in feedstuff where the protease is of the subtilisin family and/or has less than 10% residual activity when inhibited with subtilisin, is claimed. Also claimed are: improving the nutritional value of feedstuff; an animal food-additive; and treatment of vegetable proteins. At least one acid stable protease is useful in the preparation of a composition for use in feedstuff. The protease is of the subtilisin family and/or 10% residual activity when inhibited with subtilisin. The dosage of the protease is 0.01-200 mg/kg of feed. The feed composition is useful for feeding animals, including humans.

Animals include ruminants and non-ruminants i.e. monogastric animals i.e. pigs, poultry and fish. The feedstuff comprises phytase, endo-1,4-beta-D-xylanase (EC-3.2.1.8), galactanase and/or beta-glucanase (EC-3.2.1.39). Soybean (Glycine max) is included amongst the vegetable source. (63pp)

=> d his

(FILE 'HOME' ENTERED AT 10:01:46 ON 09 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:02:22 ON 09 AUG 2007

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L1      21366 S ACID (W) (RESISTANT OR STABLE)
L2      515920 S PROTEASE?
L3      85 S L1(W)L2
L4      44 DUP REM L3 (41 DUPLICATES REMOVED)
L5      6 S (CEREAL OR NUTRI? OR (PROTEIN (W)SOURCE)) AND L4
L6      1048 S NOCARDIOPSIS###
L7      130 S L2 AND L6
L8      8 S L1 AND L7
L9      4 DUP REM L8 (4 DUPLICATES REMOVED)
        E SJOEHOLM C/AU
L10     37 S E3-E4
        E OESTERGAARD P R/AU
L11     49 S E3-E9
L12     76 S L10 OR L11
L13     6 S L3 AND L12
L14     4 DUP REM L13 (2 DUPLICATES REMOVED)
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| | Document ID | Kind Codes | Source | Issue Date | Pages | Title |
|----|--------------------------|------------|--------------|------------|-------|--|
| 1 | US 2007010476 4 A1 | | US- PGPUB | 20070510 | 60 | Recombinant production of antimicrobial peptides |
| 2 | US 2006023641 4 A1 | | US- PGPUB | 20061019 | 64 | Proteases and methods for producing them |
| 3 | US 2006014749 9 A1 | | US- PGPUB | 20060706 | 43 | Proteases |
| 4 | US 2006014373 8 A1 | | US- PGPUB | 20060629 | 65 | Proteases and methods for producing them |
| 5 | US 2005005874 7 A1 | | US- PGPUB | 20050317 | 47 | Proteases |
| 6 | US 2005005574 7 A1 | | US- PGPUB | 20050310 | 36 | Proteases |
| 7 | US 2004016144 8 A1 | | US- PGPUB | 20040819 | 19 | Use of acid stable protease in animal feed |
| 8 | US 2001002679 7 A1 | | US- PGPUB | 20011004 | 18 | Use of acid-stable proteases in animal feed |
| 9 | US 7208310 B2 | | USPAT | 20070424 | 33 | Proteases |
| 10 | US 7179630 B2 | | USPAT | 20070220 | 44 | Thermostable proteases |
| 11 | US 6855548 B2 | | USPAT | 20050215 | 16 | Use of acid-stable proteases in animal feed |

| | Document ID | Kind Codes | Source | Issue Date | Pages | Title |
|----|--------------------------|------------|--------------|------------|-------|--|
| 1 | US 2007010476 4 A1 | | US- PGPUB | 20070510 | 60 | Recombinant production of antimicrobial peptides |
| 2 | US 2006023641 4 A1 | | US- PGPUB | 20061019 | 64 | Proteases and methods for producing them |
| 3 | US 2006014749 9 A1 | | US- PGPUB | 20060706 | 43 | Proteases |
| 4 | US 2006014373 8 A1 | | US- PGPUB | 20060629 | 65 | Proteases and methods for producing them |
| 5 | US 2005005874 7 A1 | | US- PGPUB | 20050317 | 47 | Proteases |
| 6 | US 2005005574 7 A1 | | US- PGPUB | 20050310 | 36 | Proteases |
| 7 | US 2004016144 8 A1 | | US- PGPUB | 20040819 | 19 | Use of acid stable protease in animal feed |
| 8 | US 2001002679 7 A1 | | US- PGPUB | 20011004 | 18 | Use of acid-stable proteases in animal feed |
| 9 | US 7208310 B2 | | USPAT | 20070424 | 33 | Proteases |
| 10 | US 7179630 B2 | | USPAT | 20070220 | 44 | Thermostable proteases |
| 11 | US 6855548 B2 | | USPAT | 20050215 | 16 | Use of acid-stable proteases in animal feed |

| | Document ID | Kind Codes | Source | Issue Date | Pages | Title |
|---|--------------------------|------------|--------------|------------|-------|--|
| 1 | US 2004016144 8 A1 | | US- PGPUB | 20040819 | 19 | Use of acid stable protease in animal feed |
| 2 | US 2003002177 4 A1 | | US- PGPUB | 20030130 | 26 | Use of acid-stable subtilisin proteases in animal feed |
| 3 | US 2001002679 7 A1 | | US- PGPUB | 20011004 | 18 | Use of acid-stable proteases in animal feed |
| 4 | US 6855548 B2 | | USPAT | 20050215 | 16 | Use of acid-stable proteases in animal feed |
| 5 | US 4473644 A | | USPAT | 19840925 | 5 | Acid stable protease from mutants of genus Rhizopus |
| 6 | US 4062732 A | | USPAT | 19771213 | 4 | Process of producing acid stable protease |

| | L # | Hits | Search Text |
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| 1 | L1 | 9258 2 | protease\$2 |
| 2 | L2 | 1077 0 | acid adj (resistant or stable) |
| 3 | L3 | 110 | l2 adj l1 |
| 4 | L4 | 209 | nocardiopsis |
| 5 | L5 | 11 | l3 same l4 |
| 6 | L6 | 8136 8 | cereal or nutrient or (protein adj source) |
| 7 | L7 | 6 | l3 same l6 |
| 8 | L8 | 9 | SJOEHOLM-CARSTEN OESTERGAARD-PETER- RAHBEK |
| 9 | L10 | 9 | l6 and l9 |
| 10 | L9 | 9 | l1 and l8 |
| 11 | L11 | 6 | l4 and l9 |

| | Document ID | Kind Codes | Source | Issue Date | Pages | Title |
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| 1 | US 2006014749 9 A1 | | US- PGPUB | 20060706 | 43 | Proteases |
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| 3 | US 2005005874 7 A1 | | US- PGPUB | 20050317 | 47 | Proteases |
| 4 | US 2004016144 8 A1 | | US- PGPUB | 20040819 | 19 | Use of acid stable protease in animal feed |
| 5 | US 2003002177 4 A1 | | US- PGPUB | 20030130 | 26 | Use of acid-stable subtilisin proteases in animal feed |
| 6 | US 2001002679 7 A1 | | US- PGPUB | 20011004 | 18 | Use of acid-stable proteases in animal feed |
| 7 | US 7179630 B2 | | USPAT | 20070220 | 44 | Thermostable proteases |
| 8 | US 6960462 B2 | | USPAT | 20051101 | 26 | Use of acid-stable subtilisin proteases in animal feed |
| 9 | US 6855548 B2 | | USPAT | 20050215 | 16 | Use of acid-stable proteases in animal feed |

| | L # | Hits | Search Text |
|----|-----|-----------|--|
| 1 | L1 | 9258 2 | protease\$2 |
| 2 | L2 | 1077 0 | acid adj (resistant or stable) |
| 3 | L3 | 110 | l2 adj l1 |
| 4 | L4 | 209 | nocardiopsis |
| 5 | L5 | 11 | l3 same l4 |
| 6 | L6 | 8136 8 | cereal or nutrient or (protein adj source) |
| 7 | L7 | 6 | l3 same l6 |
| 8 | L8 | 9 | SJOEHOLM-CARSTEN OESTERGAARD-PETER- RAHBEK |
| 9 | L9 | 9 | l1 and l8 |
| 10 | L10 | 9 | l6 and l9 |